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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,534	11/21/2003	Anthony H. Cincotta	02591/100B206-US3	3460

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EXAMINER	
AEDER, SEAN E	
ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
01/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,534	CINCOTTA ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-19 and 21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-19, and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 10/27/08 in response to the Office Action of 4/25/08 are acknowledged and have been entered.

Claim 25 has been added by Applicant.

Claims 1, 2, 4-19, and 21-25 are pending.

Claims 1, 4, and 6 have been amended by Applicant.

Claims 1, 2, 4-19, and 21-25 are currently under examination.

The following Office Action contains NEW GROUNDS of rejections.

Rejections Withdrawn

All previous rejections are withdrawn.

New Rejections

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 4-19, and 21-25 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12, 13, 28, and 30 of U.S. Patent No. 6,017,914 in view of Lin (Cancer Cells, 1991, 3(11)) or Cincotta et al (Cancer Research, 1994, 54:1249-1258).

Claim 1 of U.S. Patent 6,071,914 is drawn to a method for treating a patient suffering from a neoplasm comprising the steps of: comparing the blood prolactin level of said patient at each of a plurality of spaced apart time points during a 24-hour period to the corresponding prolactin level of a baseline prolactin level of healthy humans of the same sex as said patient; and adjusting the prolactin level of said patient to cause the patient's prolactin profile approach or conform to the baseline prolactin profile by administering a prolactin reducer to said mammal at a predetermined time, thereby inhibiting growth of said neoplasm in said human. Claim 12 of U.S. Patent 6,071,914 is drawn to the method of claim 1, further comprising administering a prolactin enhancer to said patient. Further, in order to cause the patient's prolactin profile approach or conform to the baseline prolactin profile it would be obvious to administer said prolactin enhancer just prior to or during times of peak prolactin levels in normal subjects (22:00-07:00) (see lines 55-56 of column 5 of U.S. Patent 6,071,914, in particular). Such times are "between about 19:00 and 1:00" and would adjust the daily prolactin peak of a tumor bearing mammal to peak at night. Claim 13 of U.S. Patent 6,071,914 is drawn to the method of claim 12, wherein said prolactin reducer is bromocriptine and said prolactin

enhancer is melatonin. In view of lines 44-53 of column 8 of U.S. Patent 6,071,914, melatonin is to be given at daily dosage levels ranging from about 10 micrograms to about 200 micrograms per kg of body weight per day, such a range is "about 0.5 to about 20 mg/person/day. In view of lines 12-10 of column 5 of U.S. Patent 6,071,914, prolactin is another obvious choice for a prolactin enhancer. Claim 18 of U.S. Patent 6,071,914 is drawn to a method for treating a patient suffering from a neoplasm comprising adjusting the prolactin level of said patient to cause the patient's prolactin profile to approach or conform to the baseline prolactin profile by administering a prolactin reducer to said patient at a predetermined time, thereby inhibiting the growth of said neoplasm in said human. Claim 28 of U.S. Patent 6,071,914 is drawn to the method of claim 18, wherein said method further comprises administering a prolactin enhancer to said patient. Claim 30 of U.S. Patent 6,071,914 is drawn to the method of claim 28, wherein said prolactin reducer is bromocriptine and said prolactin enhancer is melatonin.

Lin summarizes the state of the art of photodynamic therapy of malignant tumors, including the use of selective photosensitizers like phthalocyanine dyes and iodinated benzophenothiazine (pages 439-439, in particular).

Cincotta et al also teaches that photodynamic therapy is a promising new approach for the selective eradication of neoplastic tissue and further teaches the successful use of 5-ethylamino-9-diethylamino-benzo[a]phenothiazinium chloride, a benzophenoxazine analog, as a photosensitizing agent. Cincotta et al further teaches a method of treating tumors in a mammal with said photosensitizing agent and that

photodynamic therapy of EMT-6 tumors in mice with said photosensitizing agent resulted in direct tumor cell killing (see lines 50 of column 5 to line 6 of column 6, in particular).

In the absence of unexpected results, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine photodynamic therapy with phthalocyanine dyes, iodinated benzophenothiazine, or 5-ethylamino-9-diethylamino-benzo[a]phenothiazinium chloride with the patented invention of adjusting prolactin levels since each of these methods had been taught by the prior art to successfully eradicate neoplasm. Clearly, the instant situation is amenable to the type of analysis set forth in In re Kerkhoven, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Thus, one of ordinary skill in the art would have reasonably expected to successfully treat tumors using both methods combined.

In the Reply of 10/27/08, Applicant argues that unexpected results are obtained with a combination of neuroendocrine resetting therapy and PDT, compared to either therapy alone. Applicant states that Examples 1 and 2 and Figure 5 of the application demonstrate synergistic effects not described in the art when PDT is combined with NRT using a prolactin enhancer.

The arguments found in the Reply of 10/27/08 have been carefully considered, but are not deemed persuasive. In regard to arguments that unexpected synergistic

results are obtained with a combination of neuroendocrine resetting therapy and PDT, such synergistic results are not unexpected. Methods of combining PDT with neuroendocrine resetting therapy with metoclopramide (a prolactin enhancer) are anticipated by a *single prior art reference* (Werning et al (Arch. Ontolaryngol. Head Neck Surg., 7/95, 121:783-789). Werning teaches, *in a single reference*, the result that combing PDT with metoclopramide (inherently a prolactin enhancer capable of NRT) results in 100% tumor regression without re-growth. While Werning et al does not teach that metoclopramide treatment results in NRT, the prior art has already demonstrated, in a single reference, that combing PDT with metoclopramide (a prolactin enhancer) results in 100% tumor regression without re-growth.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Examiner, Art Unit 1642